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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/035,091

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Holly Hogrefe

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EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

NOTIFICATION DATE

DELIVERY MODE

08/19/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/035,091	Applicant(s) HOGREFE ET AL.	
	Examiner Richard G. Hutson	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,10-12,14,20,22-24,26 and 30-51 is/are pending in the application.
- 4a) Of the above claim(s) 23,24,26 and 30-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,10-12,14,20,22 and 36-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/9/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment of claims 1, 12, 36, 40, 44, 48, 49 and 50 in the paper of 5/19/2008, is acknowledged. Applicants' arguments filed on 5/19/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1, 3, 10-12, 14, 20, 22-24, 26, and 30-51 are still at issue and are present for examination.

Claims 23, 24, 26 and 30-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 10, 11, 12, 14, 20, 22 and 36-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection was stated in the previous office action as it applied to the previous claims. For applicants convenience the rejection is repeated herein.

As previously stated, claims 1, 3, 10, 11, 12, 14, 20, 22 and 36-51 are indefinite in that the claims each recite or refer to a "Pfu DNA polymerase except that it is mutated at an amino acid position selected from the group consisting of Y410, T542, D543, K593, Y595, Y385, G387 and G388". Reference to Y410, T542, D543, K593, Y595,

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Y385, G387 and G388 is relative to an amino acid sequence and absent a reference amino acid sequence, such a reference is indefinite. It is suggested that applicants include a reference amino acid sequence when referring to a specific amino acid position.

In response to this rejection applicants have amended the claims to recite that the "second enzyme is the wild type Pfu DNA polymerase identified at Accession No. P80061, except..." and argue the rejection as it applies to the newly amended claims.

Applicants submit that the wild type Pfu DNA polymerase was known as of Applicants' filing date and therefore, it is not necessary to recite the actual sequence or an accession number in the claims because one of skill in the art would understand the metes and bounds of the claim. Applicants submit that, Nevertheless, solely in an effort to expedite prosecution, Applicants have amended claims 1, 12, 36, 40, 44, 48, 49, and 50 to recite that the "wild type Pfu polymerase identified at Accession No. P80061". Accordingly, Applicants respectfully request that the Office withdraw this rejection.

Applicant's amendment of the claims and applicants complete argument are acknowledged and have been carefully considered, however, are found nonpersuasive for the reasons previously made of record and for those repeated herein.

Applicants submission that the wild type Pfu DNA polymerase was known as of Applicants' filing date and therefore, it is not necessary to recite the actual sequence or an accession number in the claims because one of skill in the art would understand the metes and bounds of the claim is acknowledged, but is not sufficient in overcoming the

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rejection on the basis that such a reference to an "Accession No." is considered to be "essential material", (MPEP § 608.01(p)) necessary to:

(1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;

(2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or

(3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.

This essential material is necessary to describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by second paragraph of 35 U.S.C. 112.

" Essential material " may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference. Applicants' specification reference to the above "essential material" is improper and as such the claims that require such "essential material" remain indefinite in its absence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 48-51. In response to the rejection, applicants have amended claims 48, 49 and 50 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the written description rejection together with the rejection based upon a lack of scope of enablement together on the basis that the Office has misinterpreted the claim language. Applicants submit that independent claims 48-50 recite the phrase "at least one amino acid position selected from the group consisting of" followed by a specific recitation of various amino acids/positions within an enzyme. Applicants continue to submit that this claim language is standard "Markush"-type language used in U.S. patent practice, and specifically approved by the MPEP (see MPEP § 2173.05(h)). As stated in the MPEP, claiming using a "Markush" group is a manner of claiming "a genus expressed as a group consisting of certain specified materials." Within the context of the present claims, the genus is a mutated enzyme specified as having at least one of a well-defined number of specific mutations. Applicants submit that the present claim language, and in particular the phrase "at least one", indicates to those of skill in the art that the genus described by the "Markush" group is not limited to enzymes with single mutations, but to enzymes having one or

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multiple mutations selected from the recited group. The claims clearly indicate which mutation or mutations are within the group from which mutations may be selected, and the claim language cited by the Office does not relate to mutations outside of those specifically recited in the "Markush" group.

Applicants further submit that in contrast to the clear language and meaning of the claims, in setting forth the rejection, the Office has parsed the phrase "at least one amino acid position selected from the group consisting of" into two separate and distinct phrases: "at least one" and "amino acid position selected from the group consisting of." Specifically, the Office interprets the phrase "at least" in the context of claims 48-50 "as allowing additional mutations outside the referenced positions, such that applicants have not adequately described [or enabled] this genus."

Applicants submit that doing so is improper because it is inconsistent with the clear meaning of the claim language. Applicants submit that it is also inconsistent with controlling case law from the Federal Circuit.

Applicants cite the "Meeting Held to Promote Uniform Practice In Chemical Divisions," 28 J. Pat. & Trademark Off. Soc'y 849, 852 (1946), the Federal Circuit recognized examples of qualifying language in Markush groups that was approved by the USPTO, including "and mixtures thereof" and "at least one member of the group." *Id.* Thus, as acknowledged by the Federal Circuit, it has long been common practice to use expressions like "at least one" in the context of Markush language to indicate that the claim covers one or more members of the recited Markush group. Applicants submit

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that therefore, in our case, the language 'at least one' and 'chosen from the group consisting of' in our judgment modifies the word substituent, allowing the patentee to select more than one substituent from among the Markush group. Thus, Applicants submit that the Office's interpretation of the Markush language at issue is incorrect and its position on written description and enablement moot. Rather, the correct claim interpretation must be that discussed above, which is fully consistent with U.S. law, U.S. patent regulations, and USPTO examination guidelines.

Applicant's amendment and complete argument is acknowledged and has been carefully considered, however, is found non-persuasive for claims 48-51 for the reasons previously made of record and repeated herein. The basis for this rejection is applicant's recitation in these claims to "Pfu DNA polymerase, except that it is mutated in at least one amino acid position...". Applicants continued argument that this language is standard Markush"-type language is not found persuasive. Applicant's attention is directed to that portion of that section of the MPEP to which applicants refer, which states that :

Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). *Ex parte Markush* sanctions claiming a genus expressed as a group consisting of certain specified materials.

As previously stated applicants use of the phrase "Pfu DNA polymerase, except that it is mutated in at least one amino acid position..." is the basis of the current

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rejection. It is the office's continued position that the office is not parsing the indicated phrase, but merely interpreting as broadly as is reasonable, given the art and applicant's specification.

As has been previously stated, this recited limitation of the second enzyme of the claimed kits removes the necessary structural limitations that are required to adequately describe the second enzyme which started out prior to any mutation as Pfu DNA polymerase, as identified at Accession No. Applicant's attention continues to be directed to the wording "at least", as it compares to the wording of applicant's claim 1. Such language of the instant claim is interpreted as allowing additional mutations outside the referenced positions, such that applicants have not adequately described this genus.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 48-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enzyme mixture comprising a first and second enzyme, wherein said first enzyme is a DNA polymerase or reverse transcriptase and said second enzyme is a Pfu DNA polymerase which comprises the amino acid sequence of SEQ ID NO: 19 with a mutation selected from the group consisting of Y410, T542, D543, K593, Y595, Y385, G387 and G388, does not reasonably provide enablement for an enzyme mixture comprising a first and second enzyme, wherein said

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first enzyme is a DNA polymerase or reverse transcriptase and said second enzyme is a mutant Pfu DNA polymerase except that it is mutated in at least one amino acid position selected from the group consisting of: Y410, T542, D543, K593, Y595, Y385, G387 and G388. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 48-51. In response to the rejection, applicants have amended claims 48, 49 and 50 and traverse the rejection as it applies to the newly amended claims.

As pointed out above, applicants traverse the rejection based upon a lack of scope of enablement together with the above rejection under written description on the basis that the Office has misinterpreted the claim language. Applicants continue to submit that independent claims 48-50 recite the phrase "at least one amino acid position selected from the group consisting of" followed by a specific recitation of various amino acids/positions within an enzyme. Applicants continue to submit that this claim language is standard "Markush"-type language used in U.S. patent practice, and specifically approved by the MPEP (see MPEP § 2173.05(h)). As stated in the MPEP, claiming using a "Markush" group is a manner of claiming "a genus expressed as a group consisting of certain specified materials." Within the context of the present claims, the genus is a mutated enzyme specified as having at least one of a well-defined number of specific mutations. Applicants continue to submit that the present claim language, and in particular the phrase "at least one", indicates to those of skill in

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the art that the genus described by the "Markush" group is not limited to enzymes with single mutations, but to enzymes having one or multiple mutations selected from the recited group. The claims clearly indicate which mutation or mutations are within the group from which mutations may be selected, and the claim language cited by the Office does not relate to mutations outside of those specifically recited in the "Markush" group.

Thus, Applicants submit the Office's interpretation of the language of claims 48-51 is incorrect, and its position on written description and enablement moot. For at least this reason, Applicants request that the Office reconsider and withdraw the rejection of claims 48-51 under 35 U.S.C. § 112, first paragraph.

As stated above, applicant's amendment and complete argument is acknowledged and has been carefully considered, however, is found non-persuasive for claims 48-51 for the reasons previously made of record and repeated herein. The basis for this rejection continues to be that applicant's recitation in these claims to "Pfu DNA polymerase, except that it is mutated in at least one amino acid position...". Applicants argument that this language is standard Markush"-type language is not found persuasive. Applicant's attention is directed to that portion of that section of the MPEP to which applicants refer, which states that :

Alternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B and C." See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). *Ex parte Markush* sanctions claiming a genus expressed as a group consisting of certain specified materials.

As previously stated applicants use of the phrase “Pfu DNA polymerase, except that it is mutated in at least one amino acid position...” is the basis of the current rejection. It is the office’s continued position that the office is not parsing the indicated phrase, but merely interpreting as broadly as is reasonable, given the art and applicants specification.

As has been previously stated and repeated above, this recited limitation of the second enzyme of the claimed kits removes the necessary structural limitations that are required to sufficiently enable the second enzyme which started out prior to any mutation as Pfu DNA polymerase. Applicant’s attention continues to be directed to the wording “at least”, as it compares to the wording of applicants claim 1. Such language of the instant claim is interpreted as allowing additional mutations outside the referenced positions, such that applicants have not sufficiently enabled this genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any enzyme mixture comprising any Pfu DNA polymerase with at least the specified mutations. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of enzymes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 10-12, 14, 20, 22 and 36-51 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 64-70, 75-87 of copending Application No. 10/079,241. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed enzyme mixtures of the instant application, comprising a first enzyme and a second enzyme wherein said first enzyme comprises a DNA polymerization activity and said second enzyme is a mutant Pfu DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon are anticipated by and thus obvious over the corresponding claims of copending Application No. 10/079,241, drawn to a enzyme mixture comprising a first enzyme and a second enzyme wherein said first enzyme is an Archaeal DNA

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polymerase and said second enzyme is a mutant Archaeal DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant acknowledgment of this provisional rejection is acknowledged, as well as applicant's statement of their intent of filing a terminal disclaimer as a means of overcoming the rejection at the time at which the claims are found otherwise allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rg
8/13/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652